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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/926,442	01/22/2002	Roger Nitsch	P67214US0	4254

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EXAMINER	
HAYES, ROBERT CLINTON	
ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 06/14/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/926,442	NITSCH ET AL.	
	Examiner	Art Unit	
	Robert C. Hayes, Ph.D.	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 March 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *27-49* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *27-49* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

1. The amendments filed 3/26/04 & 12/29/03 have been entered.

2. Applicant is reminded of the proper language and format for an abstract of the disclosure.

The abstract should be in narrative form and generally limited to a **single paragraph** on a separate sheet within the range of 50 to 150 words. It is important that the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the printer is limited. The **form and legal phraseology** often used in patent claims, such as "means" and "said," **should be avoided**. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

The language should be clear and concise and should not repeat information given in the title. It should avoid using phrases which can be implied, such as, "The disclosure concerns," "The disclosure defined by this invention," "The disclosure describes," etc.

3. This application filed under former 37 CFR 1.60 lacks the necessary reference to the prior application. A statement reading "This application is the National Stage of International Application No. PCT/EP00/03913, filed 05/02/00" should be entered following the title of the invention or as the first sentence of the specification. Also, the current status of all nonprovisional parent applications referenced should be included. See MPEP 201.11(III).

4. The rejection of claims 5 & 16 under 35 U.S.C. 112, second paragraph, as being indefinite for reciting a broad range or limitation together with a narrow range or limitation is withdrawn due to the cancellation of the claims.

5. The rejection of claims 14-21 under 35 U.S.C. 112, second paragraph, as being indefinite for the recitation of "selectively detects" is withdrawn due to the cancellation of the claims.

6. Applicant's arguments filed 12/29/03 have been fully considered but they are not deemed to be persuasive.

7. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

8. Claim 29 is rejected under 35 U.S.C. 101 for the same reasons made of record for cancelled claim 3 in Paper No: 9, because the claimed recitation of **"[u]se of..."**, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd. v. Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

9. Claims 27-49 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for prognosing/predicting possible "increased risk of developing Alzheimer's disease" in patients suspected of having the disease clinically (e.g., having specific MMS scores) when using a specifically defined antibody preparation to NGF and NT-3, does not reasonably provide enablement for diagnosing Alzheimer's disease using a single "neurotrophin" or for any method using unknown and uncharacterized antibody preparations that are not further

compared to appropriate reference/specifically defined age matched control values, etc. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims, for the reasons made of record for cancelled claims 1-21 in Paper No: 9 (mailed 9/25/03), and as follows.

Applicants argue on pages 8-9 of the response that defined antibodies are disclosed in Examples 1, 2 & 3 of the specification. In contrast to Applicants' assertions, examples of antibodies do not define the metes and bounds for antibodies needed to practice the instant invention, as currently claimed, especially when no closed-ended definition of antibodies for detecting NGF or for detecting unknown and undefined neurotrophins are provided within the instant specification.

Applicants then confirm that "the detection levels of NGF and/or NT-3 in the CSF from Alzheimer's patients are all different in the publications" cited by the Examiner, and further confirm that because "different antibodies, different ELISA systems" and "different standards for the standardization procedure are used in the referenced publication", "it is not unexpected that completely different sensitivities, i.e., detection limits, and hence different values are obtained". Therefore, in contrast to Applicants' assertions, a person skilled in the art would not reasonably know how to make and use the currently claimed invention precisely because it is not claimed nor specifically taught within the specification what constitutes the "same ELISA system, the same standardization, the same antibodies [to be used]" for successfully practicing the current invention. In other words, Applicants' arguments alternatively support the current rejection for lack of enablement because "it is not unexpected that completely different sensitivities, i.e.,

detection limits, and hence different values are obtained" when using "different antibodies, different ELISA systems..., different standards for the standardization procedure"; thereby, preventing one of skill in the art to know when they have successfully practice the invention as currently and broadly claimed. Likewise, undefined "reference values" mean nothing, by definition; thereby, also preventing the skilled artisan from knowing when, or if, they have successfully practiced the currently claimed invention without requiring undue experimentation to first discover how to make and use Applicants' invention after-the-fact. It is suggested that Applicants more directly claim their invention rather than merely re-iterate that previously recited.

Applicants argue on pages 10-11 of the response that "[t]o applicants' knowledge, no diagnostic test in any medical field has ever reached a 100% confirmation level". However, this is exactly what Applicants' claims encompass, as currently recited. Nevertheless, the issue remains that without structurally defining the necessary components and procedures required to practice Applicants' invention, which Applicants confirm cannot "reach a 100% confirmation level", and in which the examples provided within the instant specification contradict whether successful diagnosis or prognosis is possible within the detection levels claimed, which alternatively depend on the "completely different sensitivities, i.e., detection limits, and hence different values... obtained", one of skill in the art would not reasonably expect that the currently claimed method could result in a "method for diagnosing or prognosing Alzheimer's disease in a subject", for the vary same reasons previously made of record for cancelled claims 1-21; especially as it relates to no "controls" being defined within the claims.

Lastly, because no copy of any Giannakopoulos et al reference has been provided by Applicants for the Examiner's consideration, and because putative "Alzheimer's disease-*like* symptoms" in animals is not Alzheimer's disease, by definition, Applicants' arguments are further not persuasive. In other words, Applicants' comment that "Alzheimer's disease is not unique to humans" is simply a mischaracterization of that known within the art. Alzheimer's disease is not "Alzheimer's disease-like symptoms". Thus, Applicants' arguments are not on point.

10. Claims 27-49 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, for the reasons made of record for cancelled claims 1-21 in Paper No: 9.

It remains ambiguous what exactly the recitation a "reference value representing a known disease or health status" means in that no "known disease or health status" is stated in the claims for determining what constitutes such a "reference value", because not all "diseases or health status" are equivalent, and because what exactly constitutes an undefined "reference value" means nothing unless defined, by definition.

Second, again, since claims 30, 40 & 47 fail to define a "reference value", as recited in base claims 27, 38 & 45, respectively, it remains ambiguous whether a "reference value" of ≥ 4 pg/ml or ≥ 15 pg/ml, respectively, also "indicates a diagnosis..."; especially as it relates to putative control subjects who may eventually be "at increased risk of developing Alzheimer's disease" (e.g., see pg. 1 of the specification). In other words, what is envisioned when the reference values of the putative controls are already above these recited values? Do the controls

then have Alzheimer's disease, as defined by the current claim language? For example, see reference publications discussed in *pp* #9 above.

Third, as previously made of record and as discussed above in *pp* #9, in that Alzheimer's disease is a disease state unique to humans, it is indefinite what claim 29 is intended to claim that is separate and distinct from base claim 27, similar to that made of record for cancelled claim 6.

11. Claims 36-37 & 49 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, for the reasons made of record for cancelled claims 9-10 & 21 in Paper No: 9, and as follows.

There is no proper antecedent basis for the recitation of "one or more of said samples in said series" in claims 36 & 37, in that multiple "sample"/ "series of samples" are recited, and it is unclear what exact "sample" is being referenced.

Second, it remains indefinite for what metes and bounds entail a "treatment" when no parameters are recited in these claims for determining what constitutes a "treatment", especially when no such treatable parameters are described within the specification (i.e., as it relates to claims 36-37 & 49).

12. Claims 29 & 48-49 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, for the reasons made of record for cancelled claims 3 & 20-21 in Paper No: 9, and as follows.

In contrast to Applicants' assertions on page 14 of the response, no "active steps" are recited in the claims, nor defined within the specification for "*evaluating a treatment*", "*monitoring a progression* of Alzheimer's disease" or "*monitoring the success or failure* of a therapeutic treatment". Therefore, Applicants' arguments are moot.

In addition, similar to that previously made of record, claims 29 & 48-49 provide for the use of "the method according to claim 27" or "for use in monitoring..." in claims 48 & 49, but since the claim does not set forth any steps involved in the method/process, it remains unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced. In addition, no process steps for how or when "evaluating treatment for Alzheimer's disease"/ "monitoring a progression of Alzheimer's disease"/ "monitoring the success or failure of a therapeutic treatment..." are accomplished is recited; thereby, also being incomplete.

13. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Robert Hayes whose telephone number is (571) 272-0885. The examiner can normally be reached on Monday through Thursday, and alternate Fridays from 8:30 AM to 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz, can be reached on (571) 272-0887. The fax phone number for this Group is (703) 872-9306.

Robert C. Hayes, Ph.D.
June 8, 2004

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